Feline diabetes mellitus - etiopathogenesis

Reusch, Claudia E

Etiopathogenesis of feline diabetes mellitus

Prof. Dr. Claudia Reusch, Dipl ECVIM-CA
Clinic for Small Animal Internal Medicine, University of Zurich, Switzerland

The classification of diabetes mellitus in cats follows more or less the scheme used in human medicine. Although the etiopathogenic mechanisms may not be completely identical, the "human model" provides a guide for identification and differentiation of the various forms of the disease.

Type 1 diabetes. This type accounts for 5 – 10% of human cases and was previously known as insulin-dependent diabetes (IDDM) or juvenile-onset diabetes. Although it is commonly seen in childhood and adolescence, it can occur at any age, even in the 8th or 9th decade of life. It most commonly (> 90%) results from cellular-mediated autoimmune destruction of the β-cells leading to failure of insulin synthesis. The characteristic pathological lesion in the pancreas is the presence of mononuclear immune cells around and within the islets. The destructive process is limited to the β-cells, all other endocrine cells of the islets are spared. A major marker of autoimmune type 1 diabetes is the presence of circulating autoantibodies against glutamic acid decarboxylase (GAD65), islet antigen-2 (IA-2), insulin and zink transporter 8 (ZnT8). This type of diabetes is associated with absolute insulin deficiency. In cats, type 1-like diabetes is generally considered to be rare. Lymphocytic infiltration into the islets (insulitis) as a marker of immune-mediated disease has only been described in a few cases. Beta cell and insulin antibodies have so far not been demonstrated in newly diagnosed diabetic cats.

Type 2 diabetes. It is currently assumed that approximately 80% of diabetic cats suffer from a type 2-like diabetes mellitus. Similar to human type 2 diabetes mellitus, feline type 2 diabetes is a heterogeneous disease attributable to a combination of impaired insulin action in liver, muscle and adipose tissue (insulin resistance) and β-cell failure. Environmental as well as genetic factors are thought to play a role in the development of both defects.

Genetic factors have just started to be investigated. Most likely, similar to humans, diabetes in the cat is a polygenic disease and many genes will be associated with an increased risk for the disease. The most convincing evidence of a genetic basis comes from studies in the Burmese cat. In breeding lines from Australia, New Zealand and the UK, the frequency of diabetes mellitus is reported to be about 4 times higher in Burmese cats than in domestic cats.

One of the major risk factors for the development of diabetes in cats is obesity. Others are male gender, physical inactivity and indoor confinement, increasing age and the administration of glucocorticoids and progestagens. It has been shown that obese cats are

several times more likely to develop diabetes mellitus compared to cats with an optimal weight. Also similar to humans, it is now recognized in cats that adipose tissue is an active and complex endocrine organ. It is important to note that although obesity induces insulin resistance, not all obese cats develop diabetes mellitus. Healthy β-cells adapt to obesity and insulin resistance by increasing insulin secretion to maintain normal glucose tolerance. For diabetes to develop, there must be β-cell dysfunction leading to impaired glucose tolerance and eventually type 2 diabetes. Unfortunately, there are nearly no data on β-cell function and insulin secretion in cats during the natural development of diabetes and the big question, what exactly leads to β-cell failure under natural conditions, is unanswered until today. One long-known hypothesis concerns β-cell destruction by amyloid deposition. Only cats, humans and nonhuman primates have an amyloidogenic amino acid structure of IAPP with the potential to form amyloid depositions within the islets of the pancreas. Amyloid depositions have been found in many cats with diabetes, it is, however, also a frequent finding in non-diabetic cats.

Other specific types of diabetes (secondary diabetes mellitus). Diabetes in cats may develop as a consequence of another disease or the administration of diabetogenic drugs, such as glucocorticoids and progestins. These diseases may account for approximately up to 20% of diabetic cases in cats. Diabetes induced by glucocorticoids or progestins is relatively common. Pancreatitis has gained a lot of attention during the last years and it is now known that it is a relatively common disease in cats. The cause and effect of pancreatitis and diabetes in cats, however, is difficult to define and is largely unknown. Pancreatitis, however, seems to be a frequent co-morbidity and it is very likely that pancreatitis emerges during the course of the diabetic disease. In a substantial percentage of cats, it seems to be a clinical insignificant bystander, in others, it causes clinical signs and may render diabetic regulation at times very difficult. Pancreatitis may also play a role in the development of diabetic ketoacidosis. In contrast, hypersomatotropism (acromegaly) and hyperadrenocorticism may cause diabetes mellitus. Nearly all cats with hypersomatotropism and approximately 80% of cats with hyperadrenocorticism will develop diabetes which often times is difficult to regulate due to severe insulin resistance. Whereas hyperadrenocorticism is a rare disorder, hypersomatotropism may be present in 10 – 15% of diabetic cats. Hyperthyroidism and hyperaldosteronism are rarely associated with overt diabetes and pheochromocytoma is extremely uncommon.

REMISSION OF DIABETES IN CATS

Remission of diabetes is defined as a situation in which clinical signs disappear, blood glucose concentration normalizes and insulin treatment (or other antidiabetic drugs) can be discontinued. Those cats most likely have a type 2-like diabetes resulting from insulin resistance and β-cell dysfunction and some degree of β-cell loss. Their remaining β-cells, however, have the capacity to recover, at least in part, during treatment. One of the major mechanism behind this phenomenon most likely is the abolishment of the damaging effects of high blood glucose on β-cells (glucotoxicity). Cats which do not experience diabetic remission may be in a more advanced stage of their disease with more pronounced β-cell loss and/or a more pronounced functional defect. Diabetic remission most often occurs during the first three to four months of therapy, however, remission one year and longer after start of therapy may occasionally be seen. Published remission rates vary widely. In our institution, remission rate is between 40 – 50% provided that the cats are newly diagnosed diabetics and do not suffer from any relevant concurrent disease.

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